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Uploading C:\Stnexp4 corrupted\QUERIES\10663124.str

L4       STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS
L4                STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.


=> s l4
SAMPLE SEARCH INITIATED 18:01:30 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   1426 TO ITERATE

 70.1% PROCESSED    1000 ITERATIONS                                  2 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        26255 TO    30785
PROJECTED ANSWERS:               2 TO      158

L5             2 SEA SSS SAM L4

=> s l4 ful
FULL SEARCH INITIATED 18:01:34 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  27190 TO ITERATE

100.0% PROCESSED   27190 ITERATIONS                               10 ANSWERS
SEARCH TIME: 00.00.01

L6            10 SEA SSS FUL L4

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   155.42     324.46

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -1.47

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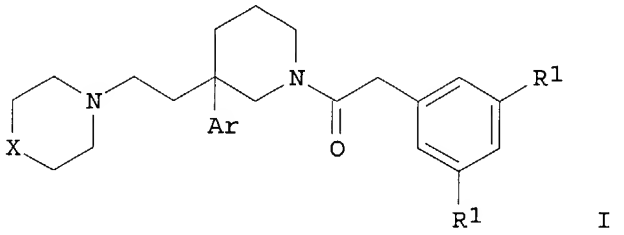
FILE COVERS 1907 - 11 Aug 2004 VOL 141 ISS 7
FILE LAST UPDATED: 10 Aug 2004 (20040810/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l6
L7 2 L6

=> d abs bib fhitstr 1-2

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
GI



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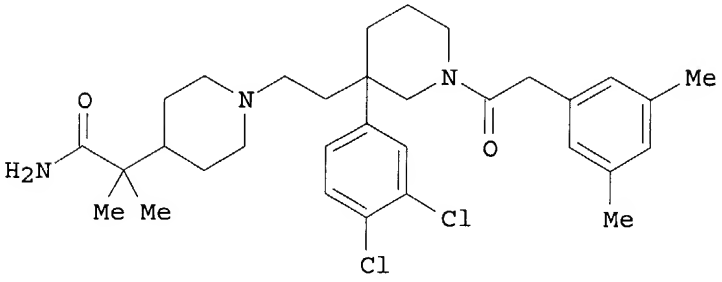


II

AB The invention relates to compds. I and their (in)organic acid salts, solvates and/or hydrates [wherein: X = NR2 or CHR2; Ar = Ph mono- or disubstituted by halo or C1-3 alkyl; R1 = Cl, Br, C1-3 alkyl, or CF3; R2 = CR3R4CONR5R6; R3, R4 = Me, Et, n-Pr, Bu; or CR3R4 forms C3-6 cycloalkyl; R5, R6 = H, C1-3 alkyl; or NR5R6 = azetidin-1-yl, pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, or perhydroazepin-1-yl]. The compds. exhibit a high affinity and high selectivity with respect to human NK1 receptors of substance P. The compds. are also orally active and demonstrate passage of the blood-brain barrier. The invention also relates to a method for production of I, intermediates useful in their production, pharmaceutical compns. containing them, and their use in the production of medicaments to treat all pathologies involving substance P and human NK1 receptors. Syntheses of 22 examples and a variety of intermediates are described. For instance, amidation of 3,5-dimethylphenylacetic acid with the (-)-isomer of 3-(3,4-dichlorophenyl)-3-(2-hydroxyethyl)piperidine, followed by Swern oxidation of the alc. to an aldehyde, and reductive

amination of this with 2-(piperidin-4-yl)isobutyramide-HCl, gave title compound (-)-II.HCl.H2O. Compds. I inhibited binding of substance P to human NK1 receptors in vitro with a Ki of approx. 10-11M, vs. 10-8M for NK2 receptors and 10-7 for NK3 receptors.

AN 2000:573786 CAPLUS

DN 133:177101

TI 1-[2-[1-(Phenylacetyl)-3-phenyl-3-piperidyl]ethyl]piperidine derivatives, method for the production thereof, and pharmaceutical compositions containing them as NK1 receptor antagonists

IN Ducoux, Jean Philippe; Emonds-Alt, Xavier; Gueule, Patrick; Proietto, Vincenzo

PA Sanofi-Synthelabo, Fr.

SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000047572	A1	20000817	WO 2000-FR284	20000208
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FR 2789389	A1	20000811	FR 1999-1593	19990210
	FR 2789389	B3	20010309		
	FR 2789390	A1	20000811	FR 1999-4429	19990407
	FR 2789390	B3	20010309		
	CA 2360894	AA	20000817	CA 2000-2360894	20000208
	BR 2000008067	A	20011106	BR 2000-8067	20000208
	EP 1150970	A1	20011107	EP 2000-903744	20000208
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	TR 200102331	T2	20020321	TR 2001-200102331	20000208
	NZ 513053	A	20021025	NZ 2000-513053	20000208
	JP 2002536442	T2	20021029	JP 2000-598492	20000208
	EE 200100417	A	20021216	EE 2001-417	20000208
	AU 763716	B2	20030731	AU 2000-25531	20000208
	RU 2220956	C2	20040110	RU 2001-121989	20000208
	ZA 2001005829	A	20020716	ZA 2001-5829	20010716
	HR 2001000566	A1	20020831	HR 2001-566	20010726
	NO 2001003878	A	20011010	NO 2001-3878	20010808
	BG 105794	A	20020531	BG 2001-105794	20010808
	US 6642233	B1	20031104	US 2001-913106	20010809
	US 2004072840	A1	20040415	US 2003-663124	20030916
PRAI	FR 1999-1593	A	19990210		
	FR 1999-4429	A	19990407		
	WO 2000-FR284	W	20000208		
	US 2001-913106	A3	20010809		

OS MARPAT 133:177101

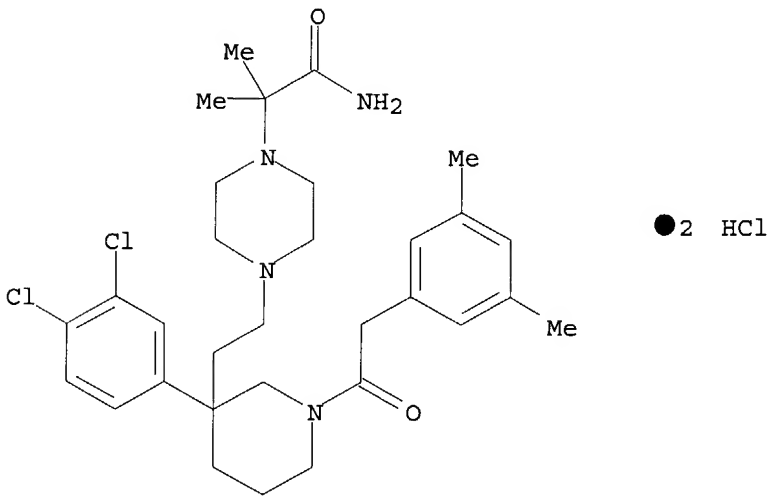
IT **288378-97-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of [[(phenylacetyl)phenylpiperidyl]ethyl]piperidine derivs. as NK1 receptor antagonists)

RN 288378-97-2 CAPLUS

CN 1-Piperazineacetamide, 4-[2-[3-(3,4-dichlorophenyl)-1-[(3,5-dimethylphenyl)acetyl]-3-piperidinyl]ethyl]-α,α-dimethyl-, dihydrochloride, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

AB To rapidly gain information on structure-activity relation (SAR) requirements of the human neurokinin 3 (hNK-3) receptor antagonist SR 142801, an indexed combinatorial library was synthesized in solution and screened on the hNK-3 receptor. SAR considerations drawn from binding affinity of combinatorial mixts. were confirmed through the synthesis and biol. evaluation of some individual compds.

AN 1999:745214 CAPLUS

DN 132:131772

TI Investigation of SAR requirements of SR 142801 through an indexed combinatorial library in solution

AU Raveglia, Luca F.; Vitali, Mauro; Artico, Marco; Graziani, Davide; Hay, Douglas W. P.; Luttmann, Mark A.; Mena, Renzo; Pifferi, Giorgio; Giardina, Giuseppe A. M.

CS Department of Medicinal Chemistry, SmithKline Beecham S.p.A., Milan, 20021, Italy

SO European Journal of Medicinal Chemistry (1999), 34(10), 825-835
CODEN: EJMCA5; ISSN: 0223-5234

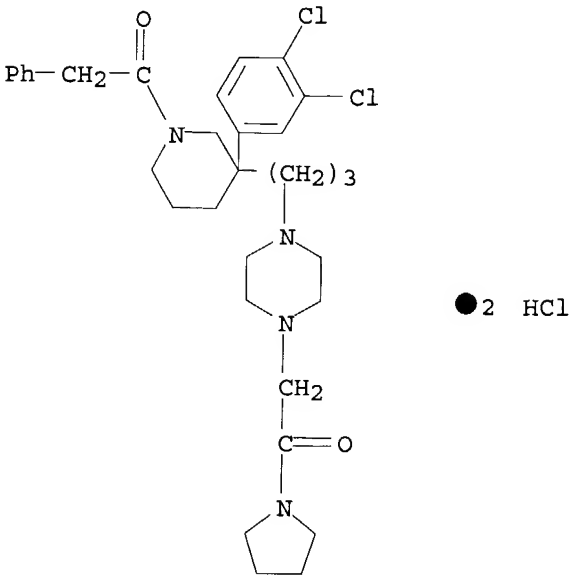
PB Editions Scientifiques et Medicales Elsevier

DT Journal

LA English

IT **256497-35-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structure-activity relation requirements of SR 142801 as neurokinin 3 receptor antagonists through indexed combinatorial library in solution)

RN 256497-35-5 CAPLUS
CN Piperidine, 3-(3,4-dichlorophenyl)-3-[3-[4-[2-oxo-2-(1-pyrrolidinyl)ethyl]-1-piperazinyl]propyl]-1-(phenylacetyl)-, dihydrochloride (9CI) (CA INDEX NAME)



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

European Journal of Medicinal Chemistry
Volume 34, Issue 10 , October 1999, Pages 825-835

doi:10.1016/S0223-5234(99)00210-X Cite or Link Using DOI

Original article

Investigation of SAR requirements of SR 142801 through an indexed combinatorial library in solution

Luca F. Raveglia[a], Mauro Vitali[c], Marco Artico[a], Davide Graziani[a], Douglas W. P. Hay[b], Mark A. Luttmann[b], Renzo Mena[a], Giorgio Pifferi[c] and Giuseppe A. M. Giardina[a]

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Received 3 May 1999; accepted 25 May 1999. Available online 9 May 2000.

Abstract

To rapidly gain information on structure-activity relationship (SAR) requirements of the human neurokinin 3 (hNK-3) receptor antagonist SR 142801, an indexed combinatorial library was synthesised in solution and screened on the hNK-3 receptor. SAR considerations drawn from binding affinity of combinatorial mixtures were confirmed through the synthesis and biological evaluation of some individual compounds.

Author Keywords: tachykinins; neurokinin 3 receptor antagonists; combinatorial chemistry; indexed libraries; structure-activity relationships

Further Reading

[14]. (a) Calculated utilising the average molecular weight. (b) Calculated as the sum of the

areas of the seven peaks of the LC/UV chromatogram, attributed by LC/MS to the seven compounds forming each mixture.

Correspondence and reprints

European Journal of Medicinal Chemistry
Volume 34, Issue 10 , October 1999, Pages 825-835

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